REMARKS

Amendments to the claims

Claims 34-42 have been amended to specify that the composition is a "pharmaceutical" composition that includes a "pharmaceutically acceptable carrier." These amendments find support in the original specification, e.g., see original claim 31.

Claim 34 has also been amended to specify that the wild-type peanut allergen is "an Ara h 1, Ara h 2, or Ara h 3 protein." As amended claim 34 also lists the SEQ ID NOs: of the nucleotide sequences that encode these proteins. These amendments find support in the original specification, e.g., see original claims 35-37.

Claims 35-37 have also been amended, as suggested by the examiner, to clarify that the SEQ ID NOs: 1-3 are nucleotide sequences, not amino acid sequences (see Sequence Listing for support).

Claims 43-45 have been added. Claim 43 is a dependent claim that specifies that the dead *E. coli* was heat-killed (e.g., see [0047], [0057] and Examples 1 and 3 of the specification for support). Claim 44 is a dependent claim that specifies that the dead *E. coli* was killed by chemical treatment. Claim 45 further specificies that the dead *E. coli* was killed using a chemical selected from the group consisting of iodine, bleach, ozone, and alcohols (e.g., see [0047] of the specification for support).

No new matter is being added.

Objection to claim 34 under 37 C.F.R. § 1.821(d)

The examiner objected to claim 34 under 37 C.F.R. § 1.821(d) because "SEQ ID NO: is required." This amendment is moot in light of the aforementioned amendments to claim 34. However, applicant respectfully submits that the examiner's objection was improper. Indeed, 37 C.F.R. § 1.821(d) simply requires claims to include a "SEQ ID NO:" when the claim refers to *"a sequence that is set forth in the 'Sequence Listing'."* Original claim 34 was a generic claim that referred to peanut allergens generally, not to a specific peanut allergen with a sequence set forth in the Sequence Listing. Original claim 34 did not therefore require a "SEQ ID NO:" as the examiner suggests.

Objection to claims 35-37

The examiner correctly noted that SEQ ID NOs: 1-3 are nucleotide sequences, not amino acid sequences. As noted, applicant has addressed this objection by amending the SEQ ID NO: references in claims 35-37.

Drawings

The examiner objected to the legends and margins of Figures 1-4. Applicant is filing appropriately corrected Figures 1-4 herewith. These figures are otherwise identical to original Figures 1-4, no new matter is being added.

Rejection for lack of enablement

Claims 34-42 were rejected for lack of enablement. In supporting this rejection, the Examiner cites *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) and argues that the invention was so unpredictable at the time of filing that a skilled person could not have made and used the claimed invention without an undue amount of experimentation. This rejection is respectfully traversed; reconsideration and withdrawal is requested.

The examiner's argument has two parts. First, the examiner argues that the immunological properties of the claimed compositions were unpredictable at the time of filing (see pages 4 and 6 of the Office Action). Second, the examiner argues that peanut allergen mutations that reduce IgE binding were also unpredictable (see pages 4-5 of the Office Action). These two parts are addressed in turn below.

Immunological properties

In arguing that the immunological properties of the claimed compositions are unpredictable, the examiner points to the examples in the specification (specifically, Examples 3 and 4). Applicant respectfully submits that the examiner does not accurately describe the contents of the examples she cites.

As discussed in the specification, microorganisms such as *E. coli* tend to produce Th1-type (i.e., non-allergic) immune reactions in individuals. In contrast, allergens such as the peanut allergens Ara h 1, 2 and 3 tend to produce Th2-type (i.e., allergic) immune reactions. Th1-type immune reactions and Th2-type immune reactions are mutually inhibitory. One aspect of the

present invention is the recognition that, by administering allergens in the context of microorganisms such as *E. coli*, it might be possible to cause a recipient individual to mount a Th1-type immune reaction to the administered allergen, and therefore to suppress any Th2-type reaction to that allergen (see specification, for example, [0041]).

The specification describes the administration of *E. coli* cells that contain the peanut allergens Ara h 1, 2 or 3 to mice. According to the Examples, high levels of IgG2a (indicative of a Th1-type response) were observed for *both* Ara h 2 and Ara h 3. High levels of IgG1 (indicative of a Th2-type response) were also observed for Ara h 2. Antibody levels were not high enough for Ara h 1 to detect whether Th2-type or Th1-type responses were occurring. Thus, the specification *exemplifies* initiation of a Th1-type immune reaction to peanut allergens Ara h 2 and Ara h 3 expressed in *E. coli*. It is true that evidence of a Th2-type reaction was also observed for Ara h 2, but that was explained as resulting from released protein which, obviously, would be expected to induce a strong Th2 response.

This simple finding is incredibly powerful. Peanut allergy is one of the most severe allergies known to man. The present inventors *demonstrated* that it is possible to cause peanut allergens to induce a non-allergic reaction merely by presenting them in the context of *E. coli* cells. The present inventors also *explained* why deviations were observed for Ara h 1 (low expression) and Ara h 2 (released protein). Those of ordinary skill in the art, armed with these teachings, would have recognized that the immunological properties of the inventive compositions are far more predictable than the examiner suggests.

Peanut allergen mutations

The claimed compositions comprise dead *E. coli* cells that contain modified peanut allergens with reduced IgE binding. The examiner argues that it would require undue experimentation to make any suitably modified peanut allergens because the selection of mutation(s) would be too unpredictable. To support this argument, the examiner points to applicant's own peptide mutational studies with Ara h 1 (Burks et al.) and Ara h 2 (Stanley et al.). Specifically, the examiner jumps on the fact that some of the Ara h 1 and Ara h 2 mutations that applicant tested *failed* to reduce IgE binding or even increased IgE binding (see page 5 of Office Action). According to this examiner, these "failures" render the mutational step so unpredictable that it would require undue experimentation to practice the claimed invention. In

fact, as far as this examiner is concerned the mutational step is rendered so unpredictable by these "failures" that a skilled person would have been unable to make a suitably modified peanut allergen without actually being given "the amino acid sequence of the modified peanut allergen [and] the cDNA encoding the corresponding modified allergen" (see page 5 of Office Action). This argument is absurd for several reasons.

First, it disregards the fact that Burks et al., Stanley et al. and the current application describe a vast number of Ara h 1, 2 and 3 mutations that *did* reduce IgE binding (e.g., see the numerous mutations that are listed in the Tables and Examples of U.S. Serial No. 09/141,220 that is incorporated by reference in [0069]). Thus, the present application explicitly enables the making of a significant number of species within the claimed genus. These "successes" would have weighed heavily against the "failures" that the examiner refers to – the level of predictability can only be assessed by considering both. The fact that the prior art and the current application demonstrate a frequency of "successes" that far outweighs the frequency of "failures" would have clearly indicated to a person of ordinary skill that the mutational step was far more predictable than the examiner suggests.

Second, the examiner's argument does not take into account the nature and amount of experimentation that would actually be required to identify suitable mutations that are not explicitly described in the application. In particular, as set forth in *Wands*, when the starting materials are readily available and the experimentation is of a *routine* nature then the level of experimentation is not undue. This is true even if a significant amount of experimentation would be required.

Here, the starting materials, including the Ara h 1, 2 and 3 sequences and IgE epitopes were all available to the public at the time of filing (e.g., see the Sequence Listing in this application and the Tables and Examples of U.S. Serial No. 09/141,220 that is incorporated by reference in [0069]). The specification further describes a number of exemplary sites within these IgE epitopes that have been shown to cause a reduction in IgE binding when mutated. Methods of preparing peptides or full length proteins that have been mutated with different amino acids and/or at different sites, and methods of screening these for reduced IgE binding were also comprehensively described in the specification. Most importantly, these preparation and screening steps were *mechanical* in nature and *routine* in the art at the time of filing. In fact, at the time of filing, a skilled person could have readily automated these steps. The steps

involved in this case are reminiscent of the steps that were involved in preparing the antibodies of *Wands*. There, the Court found that, although the technology involved preparing and then screening hybridomas to determine which, if any, secreted antibodies with the desired characteristics, "[p]ractitioners of the art [were] prepared to screen negative hybridomas in order to find one that makes the desired antibody." The Court did not quantify the required likelihood of success, but noted that even a success rate as low as 2.8% would not necessarily require a conclusion of undue experimentation. Thus, in *Wands*, there was a high probability that future efforts to generate antibodies within the claims would *not* succeed. However, the *Wands* inventors had demonstrated that success was achievable, and the steps required to repeat this success though laborious were routine. In this case, applicant has demonstrated that success can be achieved with a success rate that is at least as great as in *Wands*; the steps required for others to repeat this success with different mutations using the same peanut allergens were routine. The present case need only meet the enablement standard that was set in *Wands*. Applicant respectfully submits that the foregoing shows that the standard has been met.

Finally, the examiner's argument suggests that applicant could only have enabled the claimed invention by actually describing the amino acid (and cDNA) sequences of *every* possible modified peanut allergen with reduced IgE binding. Applicant respectfully submits that the standard proposed by the examiner would equate enablement with reduction to practice. For good reason, this is simply not the law. The whole point of the enablement requirement is that it allows patent applicants to claim inventions that are commensurate in scope with their *contribution* to the art. The examiner argues that applicant's contribution is limited to the specific mutations that are described in the specification. This is clearly unreasonable and unsupported by the facts of this case. Any skilled person would recognize that applicant's contribution to the art was much broader than this. Specifically, the skilled person would immediately realize that other suitable mutations exist and that these could be determined by routine experimentation. Under *Wands*, no more is required in order to fully enable the claimed invention.

For all of these reasons, applicant respectfully requests that the examiner reconsider and withdraw the rejection of claims 34-42 for lack of enablement.

Rejection for lack of written description

Claims 34-42 were rejected for lack of written description. This rejection is also respectfully traversed; reconsideration and withdrawal is requested.

The Examiner argues that applicant was not in possession of the claimed invention at the time of filing because the "disclosure fails to provide a representative number of species of *modified* peanut allergen [sic] containing [sic] in the dead *E. coli* to describe the claimed genus" (see page 8 of Office Action, *emphasis* added). The examiner reaches this conclusion by limiting her analysis to the specific species that applicant *reduced to practice* and *explicitly recited* in the specification, i.e., the *unmodified* peanut allergens Ara h 1, 2 and 3 expressed in dead *E. coli*. This is clearly not the legal standard under the written description requirement nor should it be. Indeed, the question is not "did applicant *reduce to practice* a representative number of species" but "was applicant in *possession* of a representative number of species." Any written description analysis must therefore take into account *all* species that are described in the application including those that were not reduced to practice.

While compositions with *E. coli* containing modified peanut allergens were not reduced to practice these species were comprehensively described in the specification. Notably, the specification explicitly stated that modified peanut allergens were preferred alternatives to unmodified peanut allergens for use in inventive compositions (see [0069]). Indeed, as stated in the specification, modified peanut allergens with reduced IgE binding present a reduced risk of causing an allergic or anaphylactic response in individuals that are treated with vaccines containing the inventive compositions. The specification also provided a detailed description of the amino acid structures of a representative number of modified peanut allergens via incorporated application U.S. Serial No. 09/141,220 (see [0069]). In particular, the specification set forth the complete sequences of Ara h 1, 2 and 3 (see Sequence Listing). The specification further set out the amino acid sequences of each of 23 IgE epitopes mapped in the Ara h 1 protein (see Table 1 of U.S. Serial No. 09/141,220), the amino acid sequence of each of 10 IgE epitopes mapped in the Ara h 2 protein (see Table 2 of U.S. Serial No. 09/141,220), and the amino acid sequence of each of 4 epitopes mapped in the Ara h 3 protein (see Table 3 of U.S. Serial No. 09/141,220). The specification also described particular alanine or methionine substitutions that were introduced into the mapped IgE binding sites, and showed that some of these substitutions resulted in decreased IgE binding (see Tables 4-6 of U.S. Serial No.

09/141,220). In discussing these data, the specification stated (see page 25, lines 11-23 of U.S. Serial No. 09/141,220):

> "The results discussed above for Ara h 1, Ara h 2, and Ara h 3 demonstrate that once an IgE binding site has been identified, it is possible to reduce IgE binding to this site by altering a single amino acid of the epitope. [...] Besides finding that many epitopes contained more than one residue critical for IgE binding, it was also determined that more than one residue type (ala or met) could be substituted at certain positions in an epitope with similar results. This allows for the design of a hypoallergenic protein that would be effective at blunting allergic reactions for a population of peanut sensitive individuals."

Thus, the specification specifically highlighted that substitutions at different positions, and with different amino acids, achieved the same results.

Despite this extensive description, the examiner rejectes the narrow claims on the ground that "without the amino acid sequence [and] the corresponding cDNA encoding said modified peanut allergen [...]" there is inadequate written description of "the structure associated with [sic] function of the 'modified peanut allergen'" (see page 8 of Office Action). In essence, the examiner is taking the position that applicant is only (if at all) entitled to claim compositions that include the specifically modified peanut allergens for which amino acid sequences have been provided. This is clearly not the law nor should it be. As previously noted, the proper legal question is not "did applicant *reduce to practice* and *explicitly recite* every modified peanut allergen that falls within the scope of the claims?" Instead, the question is "would a skilled person recognize that applicant was in *possession* of the modified peanut allergens that fall within the scope of the claims?"

While it is true that the specification does not explicitly set forth the sequences of all possible disruptions to Ara h 1, Ara h 2, and Ara h 3 IgE sites the inquiry does not and should not end there. Instead, the examiner should consider that, a skilled person, reading the specification, would understand, indeed would explicitly be told, that the presented substitutions were merely exemplary and others would work as well. A skilled artisan would appreciate that the techniques described in the specification would successfully identify all such substitutions. That is, a skilled person would understand that the inventors were in *possession* of the invention to the full scope of claims 34-42.

A claim limited to the particular substitutions that the inventors happened to have made prior to filing their patent application is virtually useless. Anybody of ordinary skill in the art could prepare a modified peanut allergen that falls outside the scope of the claim but still embodies the spirit, scope, and teachings of applicant's contribution. If the legal standard of written description in fact required verbatim recitation of every possible useful sequence, as asserted by the examiner, patent applicants would be forced to perform useless and wasteful experiments (potentially endlessly) merely to ensure that they could protect their contributions. Such a standard would eviscerate the patent system. The examiner's rejection of claims 34-42 for lack of written description should be removed.

Rejection for lack of definiteness

Claims 34-42 were rejected under 35 U.S.C. § 112, second paragraph for being indefinite. Specifically, the examiner argued that, in order to be definite, claim 34 must include a "carrier" in addition to "dead *E. coli*" because the claim preamble refers to a "composition."

Applicant respectfully disagrees with the examiner; however, in order to expedite prosecution of this case towards allowance, applicant has amended claim 34 (and thus also dependent claims 35-42) to include "a pharmaceutically acceptable carrier."

Rejection of claims 34, 36 and 38 for obviousness (Burks et al.)

Claims 34, 36 and 38 were rejected under 35 U.S.C. § 103 as being unpatentable over Burks et al. ("Burks") in view of Evans et al. ("Evans"). Specifically, the examiner cites Burks for teaching "a composition comprising *E. coli* containing therein a modified peanut allergen such as modified Ara h 2." The examiner cites Evans for teaching that "dead *E. coli* containing therein any desired antigen are efficient vehicle [sic] in terms of delivering antigens to the gut immune system." According to the examiner, Evans teaches that *E. coli* can be killed by chemical or heat treatment. The examiner then argues that it would have been obvious to produce the claimed invention by heat killing the *E. coli* of Burks according to the teachings of Evans. This rejection is respectfully traversed; reconsideration and withdrawal is requested.

Applicant initially notes that the examiner has given an inaccurate description of the teachings of Burks and Evans. As to Burks, the examiner states that the compositions comprise *E. coli*; however, there is no actual evidence in the cited reference that Burks used *E. coli* – we

are simply told that the modified Ara h 2 protein was expressed in "bacterial cells."

Similarly, Evans does not teach that "non-replicating dead *E. coli*" are efficient vaccine vehicles for "*any* desired antigen." This interpretation is far too broad. Instead, Evans teaches a highly specific vaccine against enterotoxigenic *E. coli* (ETEC) – e.g., see the title and opening paragraph on page 117. The vaccine is prepared by treating an enterotoxigenic *E. coli* strain with colicin E2 which is a potent DNA endonuclease. Once treated with colicin E2, the *E. coli* cells lose all of their DNA (and thus the ability to replicate) but retain "a normal complement of antigens, including CFA/I and enterotoxin(s)." Accordingly, the "non-replicating dead *E. coli*" of Evans is not taught as a vehicle for generic antigens as the examiner suggests but as a vehicle for specific CFA/I and enterotoxin(s) that are *endogenous* antigens of enterotoxigenic *E. coli*. As such, the Evans vaccine is a standard *attenuated* pathogenic bacterial vaccine that is designed to immunize recipients against the pathogenic bacterium *itself*.

In addition, instead of teaching the use of artificial chemicals or heat to kill *E. coli* cells, Evans actually teaches *away* from these methods. Indeed, as noted, Evans treated their *E. coli* cells with colicin E2 which is a potent DNA endonuclease. While colicin E2 could be characterized as a "chemical" it is not an artificial chemical in the same sense as newly added claim 44 that covers iodine, bleach, ozone, and alcohols. Furthermore, once treated with colicin E2, the *E. coli* cells retain "a normal complement of antigens, including CFA/I and enterotoxin(s), *unaltered by chemical- or heat treatment*." Evans et al. note on page 118 that having "antigens *unaltered by artificial* treatment" is an "important [factor] determining successful gut immunization." Thus, again the examiner's description of Evans is misleading.

Based on these narrow teachings it is unclear *how* a skilled person could actually combine the teachings of Burks and Evans to produce the claimed invention. The examiner suggests that the skilled person would take Burks' live bacterial cells expressing modified Ara h 2 and heat kill them as allegedly taught by Evans. However, as noted above, Evans teaches *away* from heat killing so this argument must fail. Thus, the only logical combinations that would have been available to a skilled person at the time of filing were:

(a) treating Burks' live bacterial cells with colicin E2 as taught by Evans; or

(b) introducing the modified Ara h 2 of Burks as a foreign antigen into the enterotoxigenic *E. coli* cells of Evans before these are killed with colicin E2.

As to combination (a), applicant respectfully notes that there is no evidence that the

bacterial cells of Burks were *E. coli* cells. Besides, even if they were *E. coli* cells, applicant fails to see *why* a skilled person would possibly have been *motivated* to treat the live cells of Burks with colicin E2. Burks explicitly teaches a method for preparing a "hypoallergenic" modified Ara h 2 *protein* vaccine (e.g., see last paragraph on page 314). This modified Ara h 2 protein is made recombinantly in bacterial cells. Once the cells have been grown and the Ara h 2 protein expressed, the cells are lysed and discarded by centrifugation (e.g., see second paragraph on page 313). Why and when would a skilled person want to treat the bacterial cells with colicin E2 in this process? Treating the cells during fermentation would reduce the yield of Ara h 2. Treating the cells once fermentation is complete would be pointless since the next step involves lysing the cells. The examiner may argue that a skilled person would want to use colicin E2 because Evans teaches that this produces a useful non-replicating bacterial vehicle. However, as noted above, this argument reads too much into the teachings of Evans. Evans teaches that the use of colicin E2 is useful in preparing a specific bacterial vaccine that includes endogenous antigens. Treatment with colicin E2 is crucial for their vaccine because it is a bacterial vaccine and the untreated bacterial cells are pathogenic. In contrast, Burks describes a *protein* based vaccine. Based on the teachings of Burks a skilled person would understand that the Ara h 2 protein portion is important while the bacterial portion is a mere production tool that can be discarded altogether. For all of these reasons, combination (a) cannot render the claims obvious.

As to combination (b), the motivation to combine the teachings is even less apparent. Certainly there would be no reason to replace the endogenous ETEC antigens with a modified peanut allergen such as Ara h 2. This would destroy the very purpose of the bacterial vaccine that is taught by Evans. In addition, there would be no apparent reason to add a modified peanut allergen such as Ara h 2 to the antigens already within the existing vaccine. Indeed, the whole purpose of Evans' vaccine is to build immunity against enterotoxigenic *E. coli*. Adding a modified peanut allergen would not improve the vaccine's ability to do this task. Accordingly there would be no motivation to make the proposed change. For all of these reasons, applicant also submits that combination (b) cannot render the claims obvious.

Finally, applicant respectfully submits that the examiner's argument is based on improper hindsight recontruction. It is imperative that the invention be viewed as it would have been perceived by those of ordinary skill in the art *at the time the invention was made*. The examiner must demonstrate that the person skilled in the art would have selected and combined the

references to produce the claimed invention *without the advanatage of hindsight or knowledge of the invention*. While hindsight is tempting it must be avoided, otherwise the test for obviousness will lose all meaning.

Based on the foregoing it is apparent that the combination of Burks and Evans fails to establish a *prima facie* case of obviousness. The examiner's rejection of claims 34, 36 and 38 under 35 U.S.C. § 103(a) in light of these references should therefore be removed.

Rejection of claims 40-42 for obviousness (Burks et al.)

Claims 40-42 were rejected under 35 U.S.C. § 103 as being unpatentable over Burks in view of Evans and further in view of Vrtala et al. ("Vrtala") or U.S. Patent No. 5,888,799 ("the '799 patent"). Vrtala and the '799 patent are secondary references that were cited solely as teaching elements or limitations that are present in dependent claims 40-42. Thus, Vrtala was cited as teaching a composition comprising *E. coli* with an allergen that is located within the *cytoplasm* (thus relevant to claim 40) and the '799 patent was cited as teaching a composition comprising *E. coli* with an allergen that is located within the *periplasm* (thus relevant to claim 41). Claim 42 was included in this rejection because "modified peanut allergen that [sic] located in the [...] the cytoplasm or periplasm would not be detect[ed] by antibody without disrupting *E. coli*."

The examiner does not point to any teachings in these secondary references that would remedy the deficiencies in the combination of Burks and Evans that were noted above. Accordingly, this rejection should be removed for the exact same reasons as above.

Rejection of claims 34-36 and 38-39 for obviousness (U.S. Patent No. 6,486,311)

Claims 34-36 and 38-39 were rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent No. 6,486,311 ("the '311 patent) in view of Evans. The teachings and deficiencies of Evans were described above. The '311 patent is cited as teaching a composition with live *E. coli* cells that contain modified Ara h 1 or Ara h 2 proteins. The '311 patent is a precursor reference to the Burks reference that was discussed above. Of note, while Burks described a modified Ara h 1 *protein* that had been expressed in a bacterial cell, the sections of the '311 patent that are referred to by the examiner (e.g., column 13, lines 21-51) refer to mutational studies that were peformed on small *synthetic peptides* that corresponded to the IgE epitopes of Ara h 1 and 2.

Thus, it is not accurate to state that the only difference between the claimed invention and the teachings of the '311 patent is that the *E. coli* in the former is dead since the '311 patent never describes a composition with live *E. coli* cells that contain modified "Ara h 1 or Ara h 2 proteins." Besides, even if the '311 patent did describe such compositions, it would teach no more than Burks did. The combination of the '311 patent and Evans would therefore still fail to establish a *prima facie* case of obviousness for the same reasons that were set forth above with respect to the combination of Burks and Evans. For this reason, applicant respectfully submits that the examiner's rejection of claims 34-36 and 38-39 under 35 U.S.C. § 103(a) in light of these references should also be removed.

Rejection of claims 40-42 for obviousness (U.S. Patent No. 6,486,311)

Claims 40-42 were rejected under 35 U.S.C. § 103 as being unpatentable over the '311 patent in view of Evans and further in view of Vrtala et al. ("Vrtala") or U.S. Patent No. 5,888,799 ("the '799 patent"). Again, Vrtala and the '799 patent are secondary references that were cited solely as teaching elements or limitations that are present in dependent claims 40-42. Thus, Vrtala was cited as teaching a composition comprising *E. coli* with an allergen that is located within the *cytoplasm* (thus relevant to claim 40) and the '799 patent was cited as teaching a composition comprising *E. coli* with an allergen that is located within the *periplasm* (thus relevant to claim 41). Claim 42 was included in this rejection because "modified peanut allergen that [sic] located in the [...] the cytoplasm or periplasm would not be detect[ed] by antibody without disrupting *E. coli*."

The examiner does not point to any teachings in these secondary references that would remedy the deficiencies in the combination of the '311 patent and Evans that were noted above. Accordingly, this rejection should also be removed for the same reasons as above.

Rejection of claims 34 and 37-39 for obviousness (Rabjohn et al.)

Claims 34 and 37-39 were rejected under 35 U.S.C. § 103 as being unpatentable over Rabjohn et al. ("Rabjohn") in view of Evans. The teachings and deficiencies of Evans were described above. Rabjohn is cited as teaching a composition with live *E. coli* cells that contain modified Ara h 3. Rabjohn is related to the '311 patent described above. Thus, while the '311 patent described peptide mutational studies for Ara h 1 and 2, Rabjohn simply describes similar

studies for Ara h 3. Again, Rabjohn only describes modified *synthetic peptides*, not compositions with live *E. coli* cells that contain a modified peanut allergen Ara h 3 as the examiner seems to imply. Again, even if Rabjohn did describe such compositions, it would teach no more than Burks did for Ara h 1. The combination of Rabjohn and Evans would therefore still fail to establish a *prima facie* case of obviousness for the same reasons that were set forth earlier with respect to the combination of Burks and Evans. For this reason, applicant respectfully submits that the examiner's rejection of claims 34 and 37-39 under 35 U.S.C. § 103(a) in light of these references should also be removed.

Rejection of claims 40-42 for obviousness (Rabjohn et al.)

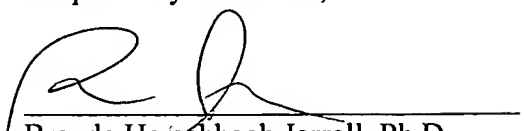
Claims 40-42 were rejected under 35 U.S.C. § 103 as being unpatentable over Rabjohn in view of Evans and further in view of Vrtala et al. ("Vrtala") or U.S. Patent No. 5,888,799 ("the '799 patent"). Again, Vrtala and the '799 patent are secondary references that were cited solely as teaching elements or limitations that are present in dependent claims 40-42. Thus, Vrtala was cited as teaching a composition comprising *E. coli* with an allergen that is located within the *cytoplasm* (thus relevant to claim 40) and the '799 patent was cited as teaching a composition comprising *E. coli* with an allergen that is located within the *periplasm* (thus relevant to claim 41). Claim 42 was included in this rejection because "modified peanut allergen that [sic] located in the [...] the cytoplasm or periplasm would not be detect[ed] by antibody without disrupting *E. coli*."

The examiner does not point to any teachings in these secondary references that would remedy the deficiencies in the combination of Rabjohn and Evans that were noted above. Accordingly, this rejection should be removed for the exact same reasons as above.

Conclusion:

For the reasons presented above, it is submitted that the examiner's rejections have been overcome and thus that the amended claims are allowable. If the examiner feels that a telephone interview would expedite the prosecution of this case towards allowance she is invited to contact the undersigned at 617-248-4793. In addition, please charge any fees that may be required, or credit any overpayment, to our Deposit Account No. 03-1721.

Respectfully submitted,



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